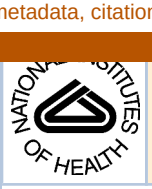

Published in final edited form as:

Am J Obstet Gynecol. 2007 September ; 197(3): 247.e1–247.e5.

The Global Network:

A Prospective Study of Stillbirths in Developing Countries

Elizabeth M MCCLURE, MEd[1], **Linda L WRIGHT, MD**[2], **Robert L GOLDENBERG, MD**[3], **Shivaprasad S GOUDAR, MD**[4], **Sailajanandan N PARIDA, MD**[5], **Imtiaz JEHAN**[6], **Antoinette TSHEFU**[7], **Elwyn CHOMBA, MBChB**[8], **Fernando ALTHABE**[9], **Ana GARCES**[10], **Hillary HARRIS, MS**[1], **Richv ard J DERMAN, MD**[11], **Pinaki PANIGRAHI, MD**[12], **Cyril ENGMANN, MD**[13], **Pierre BUEKENS, MD**[14], **Michael HAMBIDGE, MD**[15], **Waldemar A CARLO, MD**[16], and **for the NICHD FIRST BREATH Study Group***

1*Research Triangle Institute*

2*National Institute of Child Health and Human Development*

3*Drexel University*

4*Jawaharlal Nehru Medical College*

5*SCB Medical College*

6*Aga Khan University*

7*Kinshasa School of Public Health*

8*University of Zambia*

9*University of Buenos Aires*

10*San Carlos University*

11*University of Missouri - Kansas City*

12*University of Maryland Baltimore*

13*University of North Carolina at Chapel Hill*

14*Tulane School of Public Health and Tropical Medicine*

15*University of Colorado Health Sciences Center*

16*University of Alabama at Birmingham*

Abstract

Objective—Our goal was to determine stillbirth rates in a multi-site population-based study in community settings in the developing world.

Study Design—Outcomes of all community deliveries in five resource-poor countries (Democratic Republic of Congo, Guatemala, India, Zambia and Pakistan) and in one mid-level country (Argentina) were prospectively evaluated over an 18-month period. Births >1000g with no signs of life were defined as stillbirth.

Address reprint requests to: Elizabeth M McClure, Research Triangle Institute, 3040 Cornwallis Road, Durham, NC 27709, Phone: 919-316-3773, mcclure@rti.org.

Results—Outcomes of 60,324 deliveries were included. Stillbirth rates ranged from 34 per 1000 in Pakistan to 9 per 1000 births in Argentina. Increased stillbirth rates were significantly associated with lower skilled providers, out-of-hospital births, and low cesarean section rates. Maceration was present in 17.2% of stillbirths.

Conclusions—The stillbirth rates among births ≥ 1000g in these developing countries were substantially higher than reported stillbirth rates in developed countries (3-5/1000). Since most developed countries define a stillbirth as ≥20 weeks or ≥500g and since nearly half of all stillbirths are <1000g, the developing/developed country difference is actually larger than apparent from this study. Maceration was uncommon, indicating that most of the deaths probably occurred during labor. The low rates of physician attendance, hospital delivery, and cesarean sections suggest that stillbirth rates could be reduced by access to higher quality institutional deliveries.

Keywords

Stillbirth; intrapartum stillbirth; developing countries

Introduction

Stillbirths generally account for half of all perinatal mortality, with an estimated 4 million occurring worldwide each year. More than 97% of these stillbirths take place in developing countries [1]. For many reasons, stillbirths have been understudied, under reported, and rarely have been considered in attempts to improve adverse pregnancy outcomes in developing countries [1,2].

Recent estimates suggest that stillbirth rates greater than 30 per 1000 births are common among the least developed countries, especially in Sub-Saharan Africa and Southeast Asia. By comparison, rates of 3-5 per 1000 deliveries have been documented in the U.S. and other developed countries and rates of 10-15 per 1000 are reported in mid-level countries, such as those in South and Central America [3,4]. Although WHO has attempted to standardize the definition of stillbirth by recommending 1000 g as the lower limit for international comparisons (corresponding to approximately 28 weeks), the lower limit of the gestational age or birth weight reported varies widely. In developed countries, stillbirth has generally been defined as fetal loss beyond 20 weeks; however, some developed countries such as Sweden still use 28 weeks as the lower cutoff. In less developed countries, a gestational age of 28 weeks or a birth weight of 1000 grams is often the lower cutoff used[5].

The timing of stillbirth in relation to delivery also varies from developed to developing countries. Stillbirths that occur more than 12-24 hours prior to delivery have skin which is "*macerated*"[2] while those occurring in the intrapartum period or immediately prior to or during delivery are generally normal in appearance and are often called *fresh* stillbirths. In developed countries, intrapartum stillbirths comprise less than 10% of all stillbirths, while in some of the least developed countries, up to half of all stillbirths are thought to occur intrapartum[2,6]. When intrapartum stillbirths occur, they likely represent inadequate access to, or poor quality of, essential obstetric care[7,8].

Because data on stillbirths are not collected routinely in many countries, and most of the stillbirth research has been hospital-based, much is still unknown about the prevalence, timing, and circumstances associated with stillbirths in developing country where over half of all deliveries occur at home. Understanding the burden of stillbirth has important programmatic and resource implications, which are of particular concern in very low-resource settings. Our goal in this study was to determine population-based stillbirth rates and to characterize health care at delivery in prospective, well-defined community-based birth cohorts in developing country settings. Based on a review of previous studies of stillbirth [4], we hypothesized that

home birth and delivery with unskilled attendant (traditional birth attendant or family) would be associated with higher rates of stillbirth.

Methods

The study was conducted as part of the Global Network for Women's and Children's Health Research (Global Network), a National Institutes of Health-funded, multi-site research network representing partnerships of U.S. and international investigators. Prospective data registries were created to establish baseline delivery rates as part of a larger study of neonatal resuscitation in developing countries conducted in six countries: Argentina, Democratic Republic of Congo (DRC), Guatemala, India (one site in Orissa and one in Belgaum), Pakistan and Zambia. The study was reviewed and approved by the institutional ethics review committees of all participating foreign sites, the partner institutions in the U.S. and the data center, Research Triangle Institute. Consent was obtained at the community level; women provided informed verbal consent.

The outcomes of all deliveries in the communities, defined as a distinct geographic region whose birth attendants did not overlap with other communities, were collected. All birth attendants (n = 3676) were prospectively trained to collect data and assess basic clinical variables and outcomes, including differentiation of stillbirths and neonatal deaths at birth, type of stillbirth, and assessment of gestational age. Birth attendants were trained to identify maceration using pictures to standardize reporting of this condition. Data collection was overseen by trained community coordinators (nurses or physicians) who oversaw data collection of all birth attendants in the community.

Each Global Network site included ten to twenty-eight communities, with approximately 300 to 500 deliveries per community annually. The sites studied were distinct geographic entities and included rural areas in Orissa, India, Thatta, Pakistan, Kafue, Zambia and Equateur, Democratic Republic of Congo, all with very limited access to health care services, to Belgaum, India which had more access to health care, to the most developed geographic area, in Argentina.

Women were registered by 24 to 28 weeks of pregnancy. After delivery, the community coordinator collected the data recorded by the birth attendant. Data included basic information on maternal demographics, and neonatal and maternal outcomes at delivery. A stillbirth was defined as any delivery greater than or equal to 1000 g, corresponding to approximately 28 weeks gestation, in which no signs of life (breathing, crying, heartbeat, movement) were evident. The type of delivery attendant included physician, nurse or nurse-equivalent, traditional birth attendant (TBA), family or unattended. Location of delivery included hospital, health center, home (including the TBA's home) or other (in transit). Prenatal care was defined as at least one visit with a health provider. Finally, the birth weight was taken within 48 hours of delivery using scales provided for the study.

All data were entered centrally at each study site; data edits, including inter and intra-form consistency checks, were performed at entry with additional edits performed by the data center. The data were analyzed using SAS- version 9.0. Relative risks were calculated using Cochrane-Maintel-Hanszel for the prospectively identified variables associated with stillbirth. Reference categories were defined as those categories associated with the lowest stillbirth rates.

Results

From March 2005 to December 2006, 60,324 deliveries were recorded in 103 communities in the participating Global Network sites; consent was obtained from 60,154 (99.7%) women whose pregnancy outcomes were included in this study (Table I). Most women (89.0%)

received at least one prenatal care visit. In Argentina, 68.9% of the deliveries were conducted by a physician, while in three countries (Guatemala, DRC, and Zambia), less than 1% of deliveries were conducted by a physician. Most deliveries (66.3%) were conducted in a home setting (family or birth attendant's home). The site of delivery ranged from 100% of deliveries in a hospital or health clinic in Argentina to 99.9% of the deliveries in a home setting in Guatemala. Cesarean section rates ranged from 19.1% in Argentina to 0% in the communities in Guatemala and Orissa, India. Birth weights were available for 76% of stillbirths and 91% of the live births.

A total of 1472 stillbirths were recorded (Table II). The mean stillbirth rate was 24 per 1000 deliveries, ranging from 9 per 1000 in Argentina to 34 per 1000 deliveries in Pakistan. Signs of maceration were reported in 17.2% of stillbirths (range between sites was 3.6% to 45.8%). The mean birth weight for the stillbirths was 2221 g ±744 In comparison, the mean birth weight for live births was 2918±520, p = <0.001. Nearly sixty four percent (63.6%) of the stillbirths were ≥2000 g.

Women who were older than 35 years of age at delivery, had no formal education, who were primaparous or multiparous (4^{th} or greater pregnancy) had a higher relative risk of stillbirth (Table III). In addition, women who had no prenatal care, who had a lower level of care provider at delivery and delivered out of hospital were more likely to have a stillbirth than women without these characteristics. Of the perinatal characteristics, infants who were male, preterm, and < 2500 g all had a higher risk of stillbirth. Less than 1% of all stillbirths had documented congenital abnormalities at the time of delivery.

Comment

The major strength of this study was that we prospectively collected population-based delivery outcomes for distinct, geographically-defined communities in six countries, representing different levels of care. Data collectors received standardized formal training and ongoing oversight by community coordinators, who verified all pregnancy outcome data. We are not aware of any multi-country study of stillbirth with this level of data standardization or study oversight. In addition, most previous studies of stillbirths in developing countries have neither been prospective nor population-based.

The mean stillbirth rate of 24.0 per 1000 deliveries is more than five-fold higher than stillbirth rates in most developed countries. Stillbirths < 1000 g were not included in this study, but are included in the US rates and in the US account for 50% of the stillbirths [9,10]. In addition, women who did not register and experienced a stillbirth prior to 28 weeks may never have reported their loss. Thus, the disparity between the developed/developing country stillbirth rates is even larger than indicated by the comparison described above[11,12]. Within our study, stillbirth rates ranged from 9 per 1000 in the Argentinian communities to 34 per 1000 in the Pakistani communities.

Similar to studies in developed countries, maternal age > 35 and lower socio-economic status were associated with higher stillbirth rates[13]. In addition, higher stillbirth rates were associated with less prenatal care, unattended deliveries or deliveries by TBAs, out-of-hospital births, and lower rates of cesarean section. Cesarean section rates of at least 5% are considered necessary to reduce stillbirth and prevent maternal mortality[8,14,15]. Although cesarean section may be a proxy for many health care quality factors, in this study, the site with the highest cesarean section rate, Argentina, also had the lowest stillbirth rate. As another example, the Asian sites that had no access to cesarean section, Orissa, India and Thatta, Pakistan, had significantly higher stillbirth rates than Belgaum, India, which had a 3% cesarean section rate.

Because previous studies have also reported an association between lower level providers and various adverse pregnancy outcomes, ensuring increased access to skilled delivery attendants has been used in an attempt to improve adverse pregnancy outcomes[1]. However, because skilled providers are unavailable in many of the least developed geographic areas, studies have also examined a strategy of training traditional birth attendants. For example, a cluster-randomized trial in Pakistan found that training traditional birth attendants in basic delivery skills significantly reduced the stillbirth rates (50 per 1000 in the intervention clusters vs. 71 per 1000 in the control clusters)[16].

Most studies of stillbirth in developing countries have not included the birth weight, an important proxy for viability, especially where reliable gestational age dating is unavailable. Birth weight of stillbirths has been difficult to collect, often because of cultural barriers[3]. A few hospital-based studies have reported birth weight for stillbirths in less developed countries [17,18]; however, population-based stillbirth birth weights are not available. We found that the mean birth weight for stillbirths was lower than that of the live births, but more than half of the stillbirths were ≥2000 g and thus were likely to represent near-term or term deliveries. Furthermore, in this study, the majority of the stillbirths were fresh and are likely to have occurred during labor.

Acquiring more knowledge about stillbirths is important because of its significant contribution to adverse pregnancy outcomes. In this study, the mean stillbirth rate of more than 24 per 1000 represents more than a five-fold increase compared to developed country rates. Importantly, in the less developed communities, where nearly all deliveries occurred in home settings without trained health providers, rates were as high as 34 per 1000, compared to the rates in Argentina of 9 per 1000, where nearly all deliveries occurred on hospital settings. While our data suggest that higher quality of health care at delivery, especially access to high level health care providers and c-section, is associated with lower stillbirth rates, more research on the specific causes of these stillbirths would assist in planning appropriate interventions. The fact that most of the stillbirths were fresh and many were term or near-term, suggests that stillbirth rates could be substantially reduced by higher quality intrapartum care.

Acknowledgments

Supported by NIH grants from the Global Network for Women's and Children's Health Research (U01 HD040477, U01, HD0434475, U01 HD043464, U01 HD040657, U01 HD042372, U01 HD040607, U01 HD040636)

References

1. Neonatal and perinatal mortality: Country, regional and global estimates. World Health Organization; Geneva: 2006.
2. Lawn J, Shibuya K, Stein C. No cry at birth: global estimates of intrapartum stillbirth and intrapartum-related neonatal deaths. Bull World Health Organ 2005;83:409–17. [PubMed: 15976891]
3. Stanton C, Lawn JE, Rahman H, Wilczynska-Ketende K, Hill K. Stillbirth rates: delivering estimates in 190 countries. Lancet 2006;367:1487–94. [PubMed: 16679161]
4. McClure EM, Nalubamba-Phiri M, Goldenberg RL. Stillbirth in developing countries. Int J Gynaecol Obstet 2006;94(2):82–90. [PubMed: 16730726]
5. Goldenberg RL, Thompson C. The infectious origins of stillbirth. Am J Obstet Gynecol 2003;189(3): 861–73. [PubMed: 14526331]
6. Smith G. Predicting antepartum stillbirth. Curr Opin Obstet Gynecol 2006;18(6):625–30. [PubMed: 17099333]
7. Kiely JL, Paneth N, Susser M. Fetal death during labor: an epidemiologic indicator of level of obstetric care. Am J Obstet Gynecol 1985:721–6. [PubMed: 4073133]
8. Ronsmans C, De Brouwere V, Dubourg D, Dieltiens G. Measuring the need for life-saving obstetric surgery in developing countries. BJOG 2005;111:1027–1030. [PubMed: 15383102]

9. Phelan ST, Goldenberg RL, Alexander G, Cliver SP. Perinatal mortality and its relationship to the reporting of low-birthweight infants. Am J Public Health Aug;1998 88(8):1236–9. [PubMed: 9702158]
10. Kramer MS, Liu S, Luo Z, Yuan H, Platt RW, Joseph KS, et al. Analysis of perinatal mortality and its components: time for a change? Am J Epidemiol 2002;156(6):493–7. [PubMed: 12225996]
11. Silver RM, Varner MW, Reddy U, Goldenberg RL, Pinar H, Conway D, et al. Work-up of stillbirth: A review of the evidence. Amer J Obstet Gynecol 2007;196:433–44. [PubMed: 17466694]
12. Goldenberg RL, Koski JF, Boyd BW, Cutter GR, Nelson KG. Fetal deaths in Alabama 1974 to 1983: a birth weight-specific analysis. Obstet Gynecol 1987;70:831–5. [PubMed: 3684115]
13. Fretts R. Etiology and prevention of stillbirth. Am J Ob Gynec 2005;193:1923–35.
14. Stanton C, Dubourg D, DeBrouwere V, Pujades M, Ronsmans C. Reliability of data on caesarean sections in developing countries. Bull World Health Organ 2005;83(6):449–455. [PubMed: 15976896]
15. Ronsmans C, Holtz S, Stanton C. Socioeconomic differentials in caesarean rates in developing countries: a retrospective analysis. Lancet 2006;368(9546):1516–23. [PubMed: 17071285]
16. Jokhio A, Winter HR, Cheng KK. An intervention involving traditional birth attendants and perinatal and maternal mortality in Pakistan. N Engl J Med 2005;352(20):2091–9. [PubMed: 15901862]
17. Buchmann E, Pattinson RC. Babies who die from labour-related intrapartum hypoxia: a confidential enquiry in South African public hospitals. Trop Doct 2006;36(1):8–10. [PubMed: 16483418]
18. Perinatal Mortality Study Group. Perinatal mortality rate - hospital-based study during 1998-2001 at Hacettepe University. J Perinat Med 2003;31:435–440. [PubMed: 14601268]

Table I

All Deliveries: Characteristics by Study Site

Site	Total Deliveries (n)	Prenatal care (%)	Birth Attendant Type			Delivery Location		C-section (%)	Birth weight, g (mean ±SD)	≥ 2500 g (%)
			Physician (%)	Nurse (%)	TBA/ Family or Unattended (%)	Hospital or clinic (%)	Home (%)			
Argentina	6,837	90.7	68.9	31	0	100.0	0	19.1	3,303 ±549	93.8
Guatemala	6,320	85.1	0.2	34.8	54.3	0.1	99.9	0	3,204 ±537	92.5
DRC	7,952	95.3	0.1	21.6	78.3	25.6	74.4	0.1	3,045 ±567	88.1
Zambia	6,946	94.7	0.5	34.8	64.7	34.5	65.5	0.3	2,994 ±556	86.2
Orissa	10,320	87.5	3.5	42.7	53.8	5.5	94.5	0	2,607 ±278	85.7
Belgaum	11,994	98.0	31.4	30.5	38.1	51.8	48.2	2.9	2,694 ±415	79.8
Pakistan	9,785	71.5	6.2	17.7	76.1	22.8	77.2	0.1	2,717 ±481	77.7
Total	**60,154**	**89.0**	**15.8**	**26.7**	**57.5**	**33.7**	**66.3**	**2.8**	**2,901 ±542**	**85.6**

Am J Obster Gynecol. Author manuscript; available in PMC 2007 December 20.

Table II

Stillbirths: Characteristics by study site

	Stillbirths (n)	Stillbirth Rate (per 1000 births)	Macerated Stillbirth (%)	Birth weight, g (mean ± SD)	Birthweight, g			
					1000 - 1499 (%)	1500-1999 (%)	2000 - 2500 (%)	≥ 2500 g (%)
ARGENTINA	59	9	45.8	2,323±971	14.5	18.4	10.5	31.6
GUATEMALA	105	17	8.6	2,540±808	13.0	13.0	19.0	51.0
DRC	240	30	21.3	2,242±834	23.7	15.7	13.2	44.5
ZAMBIA	201	29	33.3	1,985±791	19.3	10.9	7.9	17.8
INDIA								
Orissa	280	27	3.6	2,333±371	13.3	13.3	33.3	52.0
Belgaum	257	21	26.8	2,072±546	14.1	20.3	35.0	28.2
PAKISTAN	330	34	6.1	2,257±512	11.1	11.1	27.8	50.0
Total	**1472**	**24**	**17.2**	**2,221±744**	**18.9**	**17.5**	**22.0**	**41.6**

Table III

Characteristics by Stillbirth

	Total	Stillbirths per 1000	Relative Risk (95% CI)
MATERNAL CHARACTERISTICS			
Maternal Age			
< 25	27814	22	0.9 (0.8, 1.0)
25-35*	27739	25	1.0
> 35	3625	36	1.5 (1.2, 1.8)
Education			
No formal education	26849	30	1.6 (1.4, 1.8)
Any formal education*	32639	19	1.0
Living Children			
0	14999	29	1.4 (1.2, 1.5)
1-4*	37874	21	1.0
>4	4011	29	1.4 (1.1, 1.6)
Prenatal Care			
One visit or more*	53248	22	1.0
No prenatal care	6590	44	2.0 (1.8, 2.3)
Birth attendant			
Physician*	9486	19	1.0
Nurse/Midwife	16036	25	1.3 (1.1, 1.6)
TBA/Family/Unattended	34563	26	1.3 (1.1, 1.6)
Delivery location			
Home /other	39839	26	1.2 (1.1, 1.4)
Clinic / hospital*	20282	22	1.0
INFANT CHARACTERISTICS			
Gender			
Male	31497	28	1.2 (1.0, 1.3)
Female*	28554	25	1.0
Gestational age			
< 37 weeks	7002	45	2.9 (2.5, 3.4)
≥ 37 wks*	32305	15	1.0
Birth weight			
< 2500 grams	8089	84	4.6 (4.4, 4.9)
≥ 2500 grams*	47217	7	1.0

*Reference category